the same time, we have shown (3) in an experimental model of ischemia reperfusion that T2wSTIR and T2wACUTE were significantly correlated to the AAR by pathology, but significantly overestimated it.

All of these recent publications leave the reader uncertain and confused about the utility and reliability of T_2w imaging.

In that same issue of *iJACC,* Friedrich et al. (4) boldly decided to open the debate between the AAR T_2w imaging pro and cons. As always, in such a debate, the truth probably lies somewhere in between.

What are the facts most of us agree on?

- T_2w imaging shows myocardial edema as a marker of acute injury.
- T_2w imaging is convenient and simple, can be applied retrospectively after reperfusion, and provides incremental data to delayed enhancement imaging.
- T_2w imaging and especially the classic T_2wSTIR sequence is sensitive to many artifacts that can alter the data interpretation and analysis.
- Myocardial edema detected by T_2w cardiac magnetic resonance is correlated to the myocardial AAR, although correlation does not mean causation.
- There currently are no guidelines for post-processing of T_2 hyperenhancement and association to delayed-enhancement measurement thresholds.

What are the main points of disagreement?

- T_2w imaging provides an accurate measurement of the AAR. If the definition of the AAR is purely perfusional (the area of jeopardized myocardium during the coronary occlusion), then using T_2w edema to assess the AAR assumes there is a perfect and direct relationship between the area of edema and the area of jeopardized myocardium. When we put this in a pathophysiological perspective, we know that edema is also influenced by many other factors such as microvascular obstruction, inflammation, reperfusion status, myocardial hemorrhage, reperfusion injury, and other unknown confounders. Therefore, the assumption of a direct linear relationship between the T_2w hyperenhanced area and the AAR is potentially submitted to many biases. This assumption ignores that retrospective T_2w imaging after reperfusion provides a global assessment of ischemic as well as reperfusion damage, 2 complex but cumulative and nonlinear phenomena. To accept T_2w imaging as a method of reference for the assessment of the AAR, you would have either to neglect the effect of factors other than ischemia, such as reperfusion injury, or create a new definition for the AAR.
- The place of interstitial edema in the explanation of T_2w enhancement is unclear. Friedrich et al. (4) provide a very elegant explanation of intracellular edema at the acute phase of infarction but do not mention interstitial edema. Edema in the interstitium follows a passive diffusion and would go out of the initial AAR vascular bed bounds as we showed recently (3). If the interstitial space is negligible in comparison to myocardial cells in the healthy myocardium, it increases significantly in the ischemic myocardium and is a probable major player in the well-described overestimation of infarct size by contrast-enhanced cardiac magnetic resonance at the acute phase of myocardial infarction. This is so true that early gadolinium enhancement has recently been compared in *iJACC* to T_2w imaging with acceptable levels of correlation and proposed as a new method to measure the AAR (5).

Like many others, we believe that T_2w imaging has a lot to offer for the assessment of acute myocardial infarction patients, but we have to stay close to pathophysiology and not only look at pretty pictures if we want to get closer to truth.

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REFERENCES

1. Raman SV, Ambrosio G. T_2-cardiac magnetic resonance: has Elvis left the building? Circ Cardiovasc Imaging 2011;4:198–200.
2. Fuernau G, Eitel I, Franke V, et al. Myocardium at risk in ST-segment elevation myocardial infarction comparison of T_2-weighted edema imaging with the MR-assessed endocardial surface area and validation against angiographic scoring. J Am Coll Cardiol Img 2011;4:967–76.
3. Mewton N, Rapacchi S, Augeul L, et al. Determination of the myocardial area at risk with pre- versus post-reperfusion imaging techniques in the pig model. Basic Res Cardiol 2011;106:1247–57.
4. Friedrich MG, Kim HW, Kim RJ. T_2-weighted imaging to assess post-infarct myocardium at risk. J Am Coll Cardiol Img 2011;4:1014–21.
5. Matsumoto H, Matsuda T, Miyamoto K, Shimada T, Mikuri M, Hiraoka Y. Peri-infarct zone on early contrast-enhanced CMR imaging in patients with acute myocardial infarction. J Am Coll Cardiol Img 2011;4:610–8.

REPLY

We thank Dr. Mewton and colleagues for their interest in our paper (1) and applaud them for raising an important point concerning the validity of current T2-weighted CMR imaging to visualize the area at risk in reperfused myocardial infarction (MI).

While technical issues with CMR imaging will be resolved by improved T2-weighted imaging protocols or novel T2 mapping techniques, the relationship of myocardial edema to the underlying pathophysiology deserves attention.

Recent animal data have confirmed an excellent agreement of findings in T2-weighted images with pathology in early reperfused MI (2). The amount of peri-infarct edema in clinical studies, however, varies significantly (3) and thus needs to be further studied. Specifically, there is a lack of validation data on the impact of potential confounders related to reperfusion. It is very likely that reperfusion injury with associated peri-infarct inflammation and microvascular dysfunction will modify the extent of myocardial edema. A recent study by Mewton et al. (4) indicates that reperfusion after a 40-min period of coronary occlusion may increase the extent of edema and thus apparent "myocardial salvage" within the first 90 min. Regarding late reperfusion, previous clinical studies showing edema adjacent to the necrotic

zone in late reperfused myocardial infarction (3), which is unlikely to be related to actual salvage but more likely reflects an inflammatory response of adjacent tissue, is possibly related to reperfusion injury. Moreover, in several studies, the area at risk was consistently larger in the group with more severe injury as indicated by myocardial hemorrhage (5).

Because the histologic assessment of myocardial edema is challenging and virtually impossible in clinical models, experimental and clinical research will have to use CMR and careful study designs to scrutinize the impact of reperfusion and other, less important potential confounders on the extent of myocardial edema.

Despite these knowledge gaps, there is solid evidence that T2-weighted imaging is closely correlated with the area at risk in reperfused MI and, in combination with late Gd enhancement imaging, allows for the assessment of myocardial salvage. Before having a more clear understanding of confounders, it may be too early to claim a precision in the <10% range. Clearly, further studies are required to understand the impact of potential clinical confounders, yet there is little doubt that the available techniques provide unique invaluable in vivo data on myocardial injury in patients with reperfused MI.

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REFERENCES

1. Friedrich MG, Kim HW, Kim RJ. T_2-weighted imaging to assess post-infarct myocardium at risk. J Am Coll Cardiol Img 2011;4:1014–21.
2. Beyers RJ, Smith RS, Xu Y, et al. T(2)-weighted MRI of post-infarct myocardial edema in mice. Magn Reson Med 2012;67:201–9.
3. Friedrich MG, Abdel-Aty H, Taylor A, Schulz-Menger J, Messroghli D, Dietz R. The salvaged area at risk in reperfused acute myocardial infarction as visualized by cardiovascular magnetic resonance. J Am Coll Cardiol 2008;51:1581–7.
4. Mewton N, Rapacchi S, Augeul L, et al. Determination of the myocardial area at risk with pre- versus post-reperfusion imaging techniques in the pig model. Basic Res Cardiol 2011;106:1247–57.
5. Mather AN, Fairbairn TA, Ball SG, Greenwood JP, Plein S. Reperfusion haemorrhage as determined by cardiovascular MRI is a predictor of adverse left ventricular remodelling and markers of late arrhythmic risk. Heart 2011;97:453–9.

REPLY

We thank Dr. Mewton and colleagues for adding to the discussion regarding T2-weighted cardiac magnetic resonance (CMR). Often, a candid debate will invoke strong reactions, but we are hopeful that readers of our Pro/Con article (1) with Dr. Friedrich will carefully consider the merits of the respective arguments. Here, we present our perspective on the issues raised by Dr. Mewton and colleagues.

At the outset, philosophically, we take exception to the comment that: "*As always, in such a debate truth probably relies somewhere in between.*" At issue is whether or not T2-weighted CMR depicts post-infarct myocardium at risk. Fundamentally, it can only be one or the other.

With regard to the other issues raised:

1. We agree that T2-CMR can show myocardial edema—which we believe is a marker of necrosis in the setting of acute ischemic injury.

2. We agree that T2-CMR can provide incremental data to delayed-enhancement imaging.

3. We agree that T2-short tau inversion recovery (as well as double-inversion T2-turbospin echo) is sensitive to many artifacts. These artifacts may be indistinguishable from true abnormalities and/or render images non diagnostic. As such, we believe that "classic," black-blood T2-CMR is often neither convenient nor simple.

4. We strongly disagree that myocardial edema correlates with the myocardial area at risk (AAR). As we note in our paper, (1) the fundamental problem is that the underlying physiology is incompatible with this hypothesis. With respect to water content (and many other physiological parameters), it is well-known that the post-infarct AAR is markedly heterogeneous, with the infarcted portion having 10-fold or more edema than the salvaged, viable portion. While newer pulse sequences may improve image quality, these methods will not overcome this fundamental issue.

5. We agree that from a pathophysiological perspective, assuming that there is a direct linear relationship between the AAR (simply the perfusion territory of an epicardial coronary artery) and myocardial edema is highly problematic. T2-CMR does not index perfusion, but instead reflects dynamic and complex changes occurring within infarcted myocardium, including inflammation, hemorrhage, and microvascular obstruction, among others.

6. We are puzzled regarding the comment on interstitial edema. Because the literature is quite clear that total water content is not appreciably elevated within salvaged myocardium, it is unclear how interstitial or any other form of edema can provide a mechanism for the depiction of the AAR.

7. We disagree that delayed-enhancement CMR overestimates infarct size in the acute setting. A definitive validation study (2) should take precedence over reports—even if several—in which the "evidence" is simply size differences measured on CMR datasets, often with variable image quality.

8. Finally, with regard to the possibility that the combination of "early" and conventional "late" gadolinium-enhanced CMR can depict salvaged myocardium (3), we are disheartened by the line of reasoning that afflicts this and the majority of T2-CMR reports—namely that size differences between 2 CMR depictions of the "abnormal" zone must represent a pathophysiology. Presumably, most practitioners would not assume that the consistent overestimation of left ventricular mass as measured by gradient-echo cine-CMR as compared with steady-state free precession cine-CMR reflects a new pathophysiology.

The physiological basis for interpreting "early" delayed enhancement or T2-CMR hyperintensity as the area-at-risk is poorly described and/or inconsistent with known precepts. We are left to conclude that with new imaging techniques, it is paramount that definitive pathology-based validation studies be performed. If appropriate vali-